

(FILE 'HOME' ENTERED AT 09:58:35 ON 30 NOV 2004)

FILE 'REGISTRY' ENTERED AT 10:02:29 ON 30 NOV 2004

L1 1 S QUERCETIN/CN  
L2 1 S GENISTEIN/CN

FILE 'USPATFULL, CAPLUS' ENTERED AT 10:08:16 ON 30 NOV 2004

FILE 'USPATFULL, CAPLUS, EMBASE' ENTERED AT 10:08:22 ON 30 NOV 2004

L3 1649 FILE USPATFULL  
L4 14625 FILE CAPLUS  
L5 5730 FILE EMBASE

TOTAL FOR ALL FILES

L6 22004 S QUERCETIN OR L1  
L7 135 FILE USPATFULL  
L8 45 FILE CAPLUS  
L9 23 FILE EMBASE

TOTAL FOR ALL FILES

L10 203 S L6 AND SCAR?  
L11 147 FILE USPATFULL  
L12 46 FILE CAPLUS  
L13 23 FILE EMBASE

TOTAL FOR ALL FILES

L14 216 S L6 AND (SCAR? OR CICATRI?)  
L15 18 FILE USPATFULL  
L16 24 FILE CAPLUS  
L17 16 FILE EMBASE

TOTAL FOR ALL FILES

L18 58 S L6 (1S) (SCAR? OR CICATRI?)  
L19 31 DUP REM L16-L17 (9 DUPLICATES REMOVED)  
L20 1459 FILE USPATFULL  
L21 7647 FILE CAPLUS  
L22 6243 FILE EMBASE

TOTAL FOR ALL FILES

L23 15349 S GENISTEIN OR L2  
L24 6 FILE USPATFULL  
L25 6 FILE CAPLUS  
L26 11 FILE EMBASE

TOTAL FOR ALL FILES

L27 23 S L23 (1S) (SCAR? OR CICATRI?)  
L28 14 DUP REM L25-L26 (3 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 10:24:58 ON 30 NOV 2004

=>

L6 ANSWER 5 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN

IT **Acne**

Cell differentiation

Sebum

Sunscreens

(skin care compns. containing naringenin and/or **quercetin** and retinoid)

AN 1997:609663 CAPLUS

DN 127:267821

| PATENT NO.    | KIND | DATE     | APPLICATION NO. | DATE     |
|---------------|------|----------|-----------------|----------|
| -----         | ---  | -----    | -----           | -----    |
| PI US 5665367 | A    | 19970909 | US 1996-722540  | 19960927 |

L6 ANSWER 6 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN

AB The effects of protein kinase C (PKC) activator 1-O-tetradecanoyl phorbol-13-acetate (TPA) and inhibitor 1-(5-isoquinolinylsulfonyl)-2-methylpiperazine (H-7) and **quercetin** were studied on release of tumor necrosis factor (TNF) from mouse peritoneal macrophages primed with Propionibacterium **acnes** (PA). TPA (1-100 ng/mL) and lipopolysaccharides (LPS) (1-100 ng/mL) induced the release of TNF from PA-primed mouse peritoneal macrophages in. . . dose- and time-dependent manners in vitro, and the effects of PTA and LPS were inhibited by H-7 (12.5-100  $\mu$ mol/L) or **quercetin** (6.25-25  $\mu$ mol/L) in a dose-dependent manner. After i.p. H-7 (50 mg/kg), LPS-induced release of TNF in vivo decreased significantly. These. . .

AN 1993:189733 CAPLUS

DN 118:189733

L6 ANSWER 7 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN

ST sebaceous gland inhibitor isoflavone; **acne** treatment isoflavone; **genistein acne** treatment

AN 1991:17588 CAPLUS

DN 114:17588

| PATENT NO.     | KIND | DATE     | APPLICATION NO. | DATE     |
|----------------|------|----------|-----------------|----------|
| -----          | ---  | -----    | -----           | -----    |
| PI JP 02193919 | A2   | 19900731 | JP 1989-13481   | 19890123 |

L6 ANSWER 8 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN

AB Microbicidal formulations, especially effective against P. **acnes** on the skin, contain **quercetin** (I) [117-39-5] in combination with rutin (II) [153-18-4] and/or isorhamnetin 3-O-rutinoside (III) [604-80-8]. Thus, I 0.6, II 2.0, and III. . .

ST **quercetin** isorhamnetin rutin microbicide; Propionibacterium

IT **quercetin** isorhamnetin rutin; **acne** flavonoid

Propionibacterium **acnes**  
(control of, **quercetin** and isorhamnetin rutinoside and rutin for)

IT **Acne**

(treatment of, with skin lotion containing isorhamnetin rutinoside and **quercetin** and rutin)

IT 153-18-4

RL: BIOL (Biological study)

(skin lotion containing isorhamnetin rutinoside and **quercetin** and, for **acne** treatment)

IT 604-80-8

RL: BIOL (Biological study)

(skin lotion containing **quercetin** and rutin and, for **acne** treatment)

AN 1984:460134 CAPLUS

DN 101:60134

| PATENT NO.     | KIND | DATE     | APPLICATION NO. | DATE     |
|----------------|------|----------|-----------------|----------|
| -----          | ---  | -----    | -----           | -----    |
| PI JP 59044313 | A2   | 19840312 | JP 1982-154598  | 19820907 |
| JP 02001806    | B4   | 19900112 |                 |          |

L6 ANSWER 9 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN

AB . . . disks, and it was found that the EtOH extract of flower buds of *S. japonica* showed antibacterial activity against *P. acnes*, *P. avidum*, and *Staphylococcus aureus* under weak acidic conditions. After purification of the extract, the activity was attributed to the interaction caused

by 3 components: **quercetin** (I), rutin (II), and isorhamnetin-3-rutinoside (III). When I, II, and III were applied singly, only I showed very weak activity, . . .

AN 1984:451606 CAPLUS

DN 101:51606



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Quick Search:  within [All Full-text Sources](#)  [? Search Tips](#)**Experimental Cell Research**

Volume 228, Issue 1, 10 October 1996, Pages 29-35

doi:10.1006/excr.1996.0295 [? Cite or Link Using DOI](#)  
Copyright © 1996 Academic Press, Inc. All rights reserved.**Regular Article****Integrin  $\alpha 2\beta 1$ -Dependent Contraction of Floating Collagen Gels and Induction of Collagenase Are Inhibited by Tyrosine Kinase Inhibitors**Arsi Broberg and Jyrki Heino<sup>1</sup>

MediCity Research Laboratory and Department of Medical Biochemistry, University of Turku, Tykistökatu 6A, FIN-20520, Turku, Finland

Received 29 January 1996; revised 13 June 1996. Available online 19 April 2002.

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**Abstract**

A cell culture inside a three-dimensional gel of fibrillar collagen is an experimental model used to study the response of cells to the extracellular matrix. Many cell types induce the contraction of gel and simultaneously decrease their production of type I collagen, whereas the expression of interstitial collagenase (matrix metalloproteinase-1; MMP-1) is enhanced. We have previously shown that in osteogenic cells the collagen receptor  $\alpha 2\beta 1$  integrin is a positive regulator of MMP-1 and that the number of  $\alpha 2\beta 1$  integrins on the cell surface also regulates the magnitude of contraction. However, the downregulation of collagen mRNA levels is not initiated by  $\alpha 2\beta 1$  integrin. Here, we have studied in human KHOS-240 and MG-63 osteosarcoma cells and in human skin fibroblasts the effects of tyrosine kinase inhibitors on collagen gel contraction and on the regulation of MMP-1 and collagen  $\alpha 1(I)$  genes by extracellular collagen. The induction of MMP-1 could be inhibited by all tyrosine kinase inhibitors tested with the exception of genistein. None of them could prevent the downregulation of collagen expression. Thus, the collagen-induced alterations in the expression of MMP-1 and collagen  $\alpha 1(I)$  seem to be dependent on distinct signal transduction pathways. Many of the inhibitors, including genistein, could prevent the contraction of collagen gels. The effect was not related to their ability to inhibit cell growth, because an inhibitor specific for DNA synthesis and cell division did not have the same

effect. Thus, we suggest that the process of collagen gel contraction requires protein-tyrosine phosphorylation and that the ability of cells to contract collagen gels is not related to the induction of MMP-1 or to the level of collagen  $\alpha 1(I)$  expression. Finally, we propose that the tyrosine kinase inhibitors might be considered as candidate molecules in the treatment of pathological scar contraction.

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E-mail: jyrki.heino@utu.fi.

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### **Experimental Cell Research**

Volume 228, Issue 1 , 10 October 1996, Pages 29-35

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Search Dictionary: **scar**

Search

## Meaning of SCAR

Pronunciation: skÃ¢r

Words Dictionary

### Definition:

1. [n] an indication of damage
2. [n] a mark left (usually on the skin) by the healing of injured tissue
3. [v] mark with a scar; "The skin disease scarred his face permanently"

### Websites:

- **Neosporin Scar Solution**  
Significantly improve the appearance of existing scars and help prevent the formation of scars on r wounds. Full treatment in one box. Indicated for use on raised and discolored scars.  
neosporin.com
- **CRS and E-Loe Antiaging Skin Care Program F**  
CRS and E-Loe Skin Care Products fight the seven signs of aging such as wrinkles, dull skin, large l age spots and dry skin.  
www.galaxymall.com
- **Free Scar Consultation**  
Fill in a scar consultation & discover the power of skin exfoliation to remove scars. Rebuilds & rejuvenates skin in 10 weeks results guaranteed no burning or irritation  
www.skincare-plus.com
- **Scar Products- Lowest Prices At DealTime!**  
Save time & money every time you shop online: DealTime is a free comparison-shopping service that finds the Web's best prices on links to everything from Computers & Electronics to Jewelry, Toys & more.  
www.dealtime.com
- **Vitalzym Anti Fibrosis, not Just Another Enzyme!**  
Vitalzym, Learn how Vitalzym with the Systemic enzyme Serrapeptase helps Arthritis, Lupus, Fibromyalgia, reduces inflammation and stops Fibrin from building up in the body. Wholesale prices for huge unadvertised specials!  
www.prohealthsolutions.com

**Synonyms:** cicatrice, cicatrix, mark, mark, pit, pock, scrape, scratch

**See Also:** blemish, blemish, callus, cheloid, cicatrise, cicatrize, deface, defect, disfigure, incise, keloid, pockmark, swelling, symptom, vaccination

Products Dictionary

### Definition:

Scar



Description not available.

[more details ...](#)

Webster's 1913 Dictionary

**Definition:**

1. \Scar\, n. [OF. escare, F. eschare an eschar, a dry slough (cf. It. & Sp. escara), L. eschara, fr. Gr. ? hearth, fireplace, scab, eschar. Cf. {Eschar}.]
  1. A mark in the skin or flesh of an animal, made by a wound or ulcer, and remaining after the wound or ulcer is healed; a cicatrix; a mark left by a previous injury; a blemish; a disfigurement.

This earth had the beauty of youth, . . . and not a wrinkle, scar, or fracture on all its body. --T. Burnet.

2. (Bot.) A mark left upon a stem or branch by the fall of a leaf, leaflet, or frond, or upon a seed by the separation of its support. See Illust.. under {Axillary}.

2. \Scar\, v. t. [imp. & p. p. {Scarred}; p. pr. & vb. n. {Scarring}.]  
To mark with a scar or scars.

Yet I'll not shed her blood; Nor scar that whiter skin of hers than snow. --Shak.

His cheeks were deeply scarred. --Macaulay.

3. \Scar\, v. i.  
To form a scar.

4. \Scar\, n. [Scot. scar, scaur, Icel. sker a skerry, an isolated rock in the sea; akin to Dan. ski[æ]r, Sw. sk["a"]r. Cf. {Skerry}.]  
An isolated or protruding rock; a steep, rocky eminence; a bare place on the side of a mountain or steep bank of earth. [Written also {scaur}.]

O sweet and far, from cliff and scar, The horns of Elfland faintly blowing. --Tennyson.

5. \Scar\, n. [L. scarus, a kind of fish, Gr. ska`ros.] (Zo["o"]l.)  
A marine food fish, the scarus, or parrot fish.

**Dream Dictionary**

**Definition:** Seeing a scar in your dream, symbolizes struggles and/or painful memories and bad feelings which may have entirely healed and still continue to linger in your mind. It suggests that your past still has some influence on your life. Alternatively, a scar may represent deep-seeded insecurities which may be holding you back from your goals.

**Medicine Dictionary**

**Definition:** A scar is an abnormal condition of the skin after injury. It is characterized by dense fibrotic tissue covered epidermis.



L19 ANSWER 25 OF 31 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

AB . . . is mitogenic for fibroblasts and a stimulatory factor for collagen synthesis. Objectives: We have assessed the in vitro effects of **quercetin** on proliferation, collagen synthesis and the expression of the IGF system in keloid-derived fibroblasts. Methods Fibroblasts were isolated from earlobe keloids and exposed to **quercetin** at different concentrations. The inhibitory effects of **quercetin** on fibroblast proliferation were assayed using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay, Western and Northern blot analyses. Results: **Quercetin** inhibited keloid fibroblast (KF) proliferation in a dose-dependent manner. Significant growth inhibition was observed on day 2 of culture. The . . . growth inhibition was approximately 25 µg mL(-1). Collagen 1 expression was significantly decreased while collagen 3 was almost undetectable following **quercetin** treatment. Basal levels of IGF-I receptor (IGF-IR) β subunits, p85 subunit of phosphatidylinositol 3-kinase, c-Raf, phospho-Raf-1, phosphoMEK 1/2, phospho-mitogen-activated protein kinase, phospho-Elk-1 and phospho-Akt-1 were significantly reduced when KF cells were exposed to **quercetin** for 24 h. Blocking IGF-IR activity with IGF-IR antibody or neutralizing endogenous IGF-I activity with IGF-I antibody led to significant. . . Conclusions: Because the IGF system plays an important part in fibroblast cell proliferation and collagen production, the described activities of **quercetin** on the IGF system and collagen expression may provide a novel approach for the use of **quercetin** in treatment and/or prevention of hypertrophic **scar** and keloid.

AN 2003166605 EMBASE

TI Suppression of insulin-like growth factor signalling pathway and collagen expression in keloid-derived fibroblasts by quercetin: Its therapeutic potential use in the treatment and/or prevention of keloids.

AU Phan T.T.; See P.; Tran E.; Nguyen T.T.T.; Chan S.Y.; Lee S.T.; Huynh H.

CS H. Huynh, Lab. of Molecular Endocrinology, Div. of Cell. and Molecular Research, National Cancer Centre of Singapore, Singapore 169610, Singapore. cmrthh@nccs.com.sg

SO British Journal of Dermatology, (1 Mar 2003) 148/3 (544-552).

Refs: 49

ISSN: 0007-0963 CODEN: BJDEAZ

CY United Kingdom

DT Journal; Article

FS 013 Dermatology and Venereology.

030 Pharmacology

037 Drug Literature Index

LA English

SL English

L19 ANSWER 26 OF 31 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

AB Currently accepted conservative treatments of hypertrophic **scars** are limited to steroid injections, radiation therapy, and silicone occlusive therapy. However, the use of Mederma for these problematic lesions. . . quite prevalent in the clinical setting. Little scientific evidence exists to support the efficacy of this product in reducing hypertrophic **scars**. The aim of this study was to study the effects of Mederma on hypertrophic **scars** in the rabbit hypertrophic **scar** model, allowing the histologic quantification of **scar** elevation, dermal collagen organization, vascularity, and inflammation and the gross examination of **scar** erythema. Full-thickness wounds down to cartilage, four per ear, were created in four New Zealand White rabbits, for a total of 32 **scars**. Twenty-eight days after the initial wounding, the hypertrophic **scars** were photographed, and treatment of half of the

**scars** on each ear was begun with Mederma three times per day for a total of 4 weeks. The untreated **scars** served as control **scars** and were left exposed to air. After 4 weeks of treatment, the **scars** were once again photographed. The rabbits were then killed, and the **scars** were analyzed histologically. The pretreatment and posttreatment photographs were compared by using computer quantification of magenta, yellow, and cyan expression within the **scars**. Histologic analysis demonstrated no significant reduction in **scar** hypertrophy or **scar** elevation index. However, a significant improvement in dermal collagen organization was noted on comparing Mederma-treated **scars** with untreated control **scars** ( $p < 0.05$ ). No significant difference in dermal vascularity or inflammation was noted. Computer analysis of the **scar** photographs demonstrated no significant reduction in **scar** erythema with Mederma treatment. The active product in Mederma, allium cepa, has as its derivative **quercetin**, a bioflavonoid noted for its antiproliferative effects on both normal and malignant cells, and its antihistamine release effects. These properties could theoretically prove beneficial in reversing the inflammatory and proliferative responses noted in hypertrophic **scars**. Despite the authors' inability to demonstrate a reduction in **scar** hypertrophy, the improvement in collagen organization noted in the Mederma-treated **scars** suggests it may have an effect on the pathophysiology of hypertrophic **scar** formation.

AN 2002229561 EMBASE  
 TI Effect of Mederma on hypertrophic scarring in the rabbit ear model.  
 AU Saulis A.S.; Mogford J.H.; Mustoe T.A.  
 CS Dr. T.A. Mustoe, Division of Plastic Surgery, Northwestern Memorial Hospital, Galter Pavilion, 675 North Saint Claire, Chicago, IL 60611, United States. tmustoe@nmh.org  
 SO Plastic and Reconstructive Surgery, (2002) 110/1 (177-183).  
 Refs: 20  
 ISSN: 0032-1052 CODEN: PRSUAS  
 CY United States  
 DT Journal; Article  
 FS 009 Surgery  
 013 Dermatology and Venereology  
 037 Drug Literature Index  
 LA English  
 SL English

L29 ANSWER 98 OF 191 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 6  
 AN 1999:135047 CAPLUS  
 DN 130:279811  
 ED Entered STN: 03 Mar 1999  
 TI Lysophosphatidic acid-induced calcium mobilization and proliferation in kidney proximal tubular cells  
 AU Dixon, Richard J.; Young, Ken; Brunskill, Nigel J.  
 CS Department of Cell Physiology and Pharmacology, Leicester University School of Medicine, Leicester, LE1 9HN, UK  
 SO American Journal of Physiology (1999), 276(2, Pt. 2), F191-F198  
 CODEN: AJPHAP; ISSN: 0002-9513  
 PB American Physiological Society  
 DT Journal  
 LA English  
 CC 13-6 (Mammalian Biochemistry)  
 AB Patients with proteinuria tend to develop progressive renal disease with proximal tubular cell atrophy and interstitial **scarring**. It has been suggested that the nephrotoxicity of albuminuric states may be due to the protein mol. itself or by lipids, such as lysophosphatidic acid (LPA), that albumin carries. LPA was found to cause a transient increase in intracytoplasmic free  $\text{Ca}^{2+}$  ( $[\text{Ca}^{2+}]_i$ ) in opossum kidney proximal tubule cells (OK) that was maximal at 100  $\mu\text{M}$  LPA and was dose dependent with an  $\text{EC}_{50}$  of  $2.6 \times 10^{-6}$  M. This  $\text{Ca}^{2+}$  mobilization was from both internal stores and across the plasma membrane and was pertussis toxin (PTX) insensitive. Treatment of OK cells with 100  $\mu\text{M}$  LPA for 5 min was found to cause a twofold increase in  $[\text{H}]$ thymidine incorporation and a three- to fivefold increase over control after 24 h. This was highly PTX sensitive and insensitive to pretreatment with the tyrosine kinase inhibitors **genistein** and herbimycin A. These findings may be of significance in the progression of renal disease and indicate the potential importance of lipids in modulating proximal tubule cell function and growth.  
 ST lysophosphatidate calcium proliferation kidney proximal tubule  
 IT Animal cell line  
 (OK; lysophosphatidic acid-induced calcium mobilization and proliferation in kidney proximal tubular cells)  
 IT Cell proliferation  
 Signal transduction, biological  
 (lysophosphatidic acid-induced calcium mobilization and proliferation in kidney proximal tubular cells)  
 IT Lysophosphatidic acids  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 (lysophosphatidic acid-induced calcium mobilization and proliferation in kidney proximal tubular cells)  
 IT G proteins (guanine nucleotide-binding proteins)  
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (pertussis toxin-insensitive; lysophosphatidic acid-induced calcium mobilization and proliferation in kidney proximal tubular cells)  
 IT G proteins (guanine nucleotide-binding proteins)  
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (pertussis toxin-sensitive; lysophosphatidic acid-induced calcium mobilization and proliferation in kidney proximal tubular cells)  
 IT Kidney  
 (proximal tubule; lysophosphatidic acid-induced calcium mobilization and proliferation in kidney proximal tubular cells)  
 IT Albumins, biological studies  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(serum; lysophosphatidic acid-induced calcium mobilization and proliferation in kidney proximal tubular cells)

IT 80449-02-1, Protein tyrosine kinase  
 RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)  
 (lysophosphatidic acid-induced calcium mobilization and proliferation in kidney proximal tubular cells)

IT 9002-64-6, Parathormone 62229-50-9, EGF  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 (lysophosphatidic acid-induced calcium mobilization and proliferation in kidney proximal tubular cells)

IT 7440-70-2, Calcium, biological studies  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (lysophosphatidic acid-induced calcium mobilization and proliferation in kidney proximal tubular cells)

IT 7440-70-2, Calcium, biological studies  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

L29 ANSWER 99 OF 191 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 7  
 AN 1996:736530 CAPLUS  
 DN 126:29610  
 ED Entered STN: 14 Dec 1996  
 TI Integrin  $\alpha 2\beta 1$ -dependent contraction of floating collagen gels  
 and induction of collagenase are inhibited by tyrosine kinase inhibitors  
 AU Broberg, Arsi; Heino, Jyrki  
 CS MediCity Research Lab. Dep. Med. Biochemistry, Univ. Turku, Turku,  
 FIN-20520, Finland  
 SO Experimental Cell Research (1996), 228(1), 29-35  
 CODEN: ECREAL; ISSN: 0014-4827  
 PB Academic  
 DT Journal  
 LA English  
 CC 13-6 (Mammalian Biochemistry)  
 AB A cell culture inside a three-dimensional gel of fibrillar collagen is an  
 exptl. model used to study the response of cells to the extracellular  
 matrix. Many cell types induce the contraction of gel and simultaneously  
 decrease their production of type I collagen, whereas the expression of  
 interstitial collagenase (matrix metalloproteinase-1; MMP-1) is enhanced.  
 The authors have previously shown that in osteogenic cells the collagen  
 receptor  $\alpha 2\beta 1$  integrin is a pos. regulator of MMP-1 and that  
 the number of  $\alpha 2\beta 1$  integrins on the cell surface also regulates  
 the magnitude of contraction. However, the downregulation of collagen  
 mRNA levels is not initiated by  $\alpha 2\beta 1$  integrin. Here, the  
 authors have studied in human KHOS-240 and MG-63 osteosarcoma cells and in  
 human skin fibroblasts the effects of tyrosine kinase inhibitors on  
 collagen gel contraction and on the regulation of MMP-1 and collagen  
 $\alpha 1(I)$  genes by extracellular collagen. The induction of MMP-1 could  
 be inhibited by all tyrosine kinase inhibitors tested with the exception  
 of **genistein**. None of them could prevent the downregulation of  
 collagen expression. Thus, the collagen-induced alterations in the  
 expression of MMP-1 and collagen  $\alpha 1(I)$  seem to be dependent on  
 distinct signal transduction pathways. Many of the inhibitors, including  
**genistein**, could prevent the contraction of collagen gels. The  
 effect was not related to their ability to inhibit cell growth, because an  
 inhibitor specific for DNA synthesis and cell division did not have the  
 same effect. Thus, the authors suggest that the process of collagen gel  
 contraction requires protein-tyrosine phosphorylation and that the ability  
 of cells to contract collagen gels is not related to the induction of  
 MMP-1 or to the level of collagen  $\alpha 1(I)$  expression. Finally, the  
 authors propose that the tyrosine kinase inhibitors might be considered as  
 candidate mols. in the treatment of pathol. **scar** contraction.  
 ST collagen contraction collagenase tyrosine kinase integrin  
 IT Extracellular matrix  
 Second messenger system  
 (integrin  $\alpha 2\beta 1$ -dependent contraction of floating collagen  
 gels and induction of collagenase are inhibited by tyrosine kinase  
 inhibitors)  
 IT Collagens, biological studies  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL  
 (Biological study); PROC (Process)  
 (type I; integrin  $\alpha 2\beta 1$ -dependent contraction of floating  
 collagen gels and induction of collagenase are inhibited by tyrosine  
 kinase inhibitors)  
 IT Integrins  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL  
 (Biological study); PROC (Process)  
 ( $\alpha 2\beta 1$ ; integrin  $\alpha 2\beta 1$ -dependent contraction of  
 floating collagen gels and induction of collagenase are inhibited by  
 tyrosine kinase inhibitors)  
 IT 80449-02-1, Kinase (phosphorylating), protein (tyrosine)  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); BIOL (Biological study)  
(integrin  $\alpha 2\beta 1$ -dependent contraction of floating collagen  
gels and induction of collagenase are inhibited by tyrosine kinase  
inhibitors)

IT 9001-12-1, Collagenase

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL  
(Biological study); PROC (Process)

(integrin  $\alpha 2\beta 1$ -dependent contraction of floating collagen  
gels and induction of collagenase are inhibited by tyrosine kinase  
inhibitors)

RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L36 ANSWER 70 OF 149 USPATFULL on STN

SUMM In some of its method aspects, the present invention provides methods for **treating** cardiovascular disease, **treating** inflammatory disease, accelerating wound healing, **decreasing scarring** during wound healing, and **preventing** tumor angiogenesis and/or metastasis comprising administering to a subject in need of such **treatment** an effective amount of at least one peptide or compound based on a thrombin receptor sequence.

DRWD FIG. 6 illustrates the effects of **genistein** and indomethacin on the actions of P5-NH.sub.2 and carbachol in the RLM assay.

DETD . . . the healing process. The acceleration of wound healing would also prove of value in the use of skin grafts for **treating** burn patients and in **treatment** of ocular injuries. It is likely that thrombin itself, generated at the site of injury, plays an important role in. . . healing process; alternatively, in some situations, one might wish to delay the healing process to avoid the formation of inappropriate **scarring**, leading to the formation of cheloid. Thus, for sites of injury and tissue repair, it could prove of use to. . . antagonists, depending on the situation. A non-degradable super-active analogue of the thrombin receptor peptide may be preferably used for such **treatment** in both humans and animals. The agents may also be used in the therapy of duodenal, ileal and colonic ulcer. . .

DETD . . . action of P5 in the GLM preparation was also selectively blocked by relatively low concentrations of the tyrosine kinase inhibitors, **genistein** (GS) and tyrphostin (TP) (14). We wished to determine if the active P5 analogues modified at the C-and N-terminus (represented by. . . E, F, G and H), the contractile actions of both P5--NH.sub.2 and Pr-P4 were blocked by either indomethacin or tyrphostin; **genistein** was similarly effective (not shown). Because of the desensitization caused by Pr-P4, in the experiments shown for the GLM in. . . tissue sensitivity to TRPs was evaluated by exposure to P5--NH.sub.2 (5 µg/mL; 7.8 µM) before determining the effects of tyrphostin, **genistein** and indomethacin on Pr-P4 action (G, H, FIG. 5). In contrast, the responses of the RA, which were abolished with. . . in FIG. 6, the response of the RLM preparation to P5-NH.sub.2 was also quite sensitive to tyrphostin (not shown) and **genistein** (77±3% inhibition: mean ±S.E.M for n=6) but was only partially affected by indomethacin (40±6% inhibition: mean ±S.E.M. for n=6). In. . .

DETD . . . indomethacin, noradrenaline and angiotensin-II and thrombin (human, 3000 to 4000 U/mg; 1 U/mL.perspectiveto.10 nM) were from Sigma (St. Louis, Mo.); **genistein** (GS) was from ICN Biochemicals, Costa Mesa, Calif. Tyrphostin (TP) (RG 50864, also designated AG213) was obtained through the courtesy of Dr. R. R. Swillo, Rhone-Poulenc Rorer (Collegeville, Pa). **Genistein** and tyrphostin were dissolved in dimethylsulfoxide (DMSO) to yield a stock solution that, when diluted, resulted in a concentration of. . .

PI US 5516889 19960514

DETD Anti-acne actives can be effective in **treating** acne vulgaris, a chronic disorder of the pilosebaceous follicles. The condition involves inflammation of the pilosebaceous apparatus thereby resulting in lesions, which may include papules, pustules, cysts, comedones, and severe **scarring**. The bacteria, *Corynebacterium* acnes and *Staphylococcus epidermidis* are usually present in the pustular contents.

from Laboratories Serobiologiques); formononetin; forsythia fruit extract; gallic acid esters; gamma butyric acid; GATULINE RC (available from Gattlefosse, located in Priest, France); **genistein**; genisteine; genistic acid; ginkgo bilboa extracts; ginseng extracts; ginsenoside (R0, R6-., R6-2, R6-3, Rc, RD, RE] RP RF]29 P16-1] RG-2); gluco pyranosyl-1-ascorbate; glutathione.

ACCESSION NUMBER: 1999055303 PCTFULL ED 20020515  
 TITLE (ENGLISH): CLEANSING ARTICLES FOR SKIN AND/OR HAIR WHICH ALSO DEPOSITS SKIN CARE ACTIVES  
 TITLE (FRENCH): PRODUITS D'HYGIENE POUR LA PEAU ET/OU LES CHEVEUX DEPOSANT DE PLUS DES INGREDIENTS ACTIFS TRAITANT LA PEAU  
 INVENTOR(S): ALBACARYS, Lourdes, Dessus; McATEE, David, Michael; DECKNER, George, Endel  
 PATENT ASSIGNEE(S): THE PROCTER & GAMBLE COMPANY; ALBACARYS, Lourdes, Dessus; McATEE, David, Michael; DECKNER, George, Endel  
 LANGUAGE OF PUBL.: English  
 DOCUMENT TYPE: Patent  
 PATENT INFORMATION:

| NUMBER     | KIND | DATE     |
|------------|------|----------|
| WO 9955303 | A1   | 19991104 |

DESIGNATED STATES  
 W:

AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE  
 DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN  
 IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN  
 MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR  
 TT UA UG US UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ UG  
 ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI  
 FR GB GR IE IT LU MC NL PT SE BE BJ CF CG CI CM GA GN  
 GW ML MR NE SN TD TG

APPLICATION INFO.: WO 1999-1B635 A 19990412  
 PRIORITY INFO.: US 1998-60/083,015 19980424



L36 ANSWER 59 OF 149 USPATFULL on STN  
ACCESSION NUMBER: 2001:229235 USPATFULL  
TITLE: METHOD FOR USING SOLUBLE CURCUMIN TO INHIBIT  
PHOSPHORYLASE KINASE IN INFLAMMATORY DISEASES  
INVENTOR(S): HENG, MADALENE C.Y., NORTHRIDGE, CA, United States

|  | NUMBER  | KIND | DATE         |
|--|---|------|--------------|
| PATENT INFORMATION:                        | US 2001051184   | A1   | 20011213     |
| APPLICATION INFO.:                         | US 1999-315856  | A1   | 19990520 (9) |
| DOCUMENT TYPE:                             | Utility   |      |              |
| FILE SEGMENT:                              | APPLICATION   |      |              |
| LEGAL REPRESENTATIVE:                      | ATTN: DAVID A. FARAH. M.D., SHELDON & MAK, 225 SOUTH<br>LAKE AVENUE, SUITE 900, PASADENA, CA, 91101 |      |              |
| NUMBER OF CLAIMS:                          | 115   |      |              |
| EXEMPLARY CLAIM:                           | 1   |      |              |
| NUMBER OF DRAWINGS:                        | 13 Drawing Page(s)  |      |              |
| LINE COUNT:                                | 4191  |      |              |
| CAS INDEXING IS AVAILABLE FOR THIS PATENT. |   |      |              |

rs ,

inflammatory diseases and disorders, pyogenic granuloma, scleroderma, synovitis, trachoma and vascular adhesions.

DETD . . . and even antioxidants (U.S. Pat. No. 5,571,523; incorporated herein by reference) may also be used. Tyrosine kinase inhibitors, such as **genistein**, may also be linked to the agents of the present invention that target the cell surface receptor, VEGFR1 (as supported.

DETD The present invention may be used to **treat** animals and patients with aberrant angiogenesis, such as that contributing to a variety of diseases and disorders. The most prevalent and/or clinically important of these, outside the field of cancer **treatment**, include arthritis, rheumatoid arthritis, psoriasis, atherosclerosis, diabetic retinopathy, age-related macular degeneration, Grave's disease, vascular restenosis, including restenosis following angioplasty, arteriovenous. . . meningioma, hemangioma and neovascular glaucoma. Other potential targets for intervention include angiofibroma, atherosclerotic plaques, corneal graft neovascularization, hemophilic joints, hypertrophic **scars**, osler-weber syndrome, pyogenic granuloma retrolental fibroplasia, scleroderma, trachoma, vascular adhesions, synovitis, dermatitis, various other inflammatory diseases and disorders, and even endometriosis. Further diseases and disorders that are **treatable** by the invention, and the unifying basis of such angiogenic disorders, are set forth below.

ACCESSION NUMBER: 2002:19058 USPATFULL  
TITLE: Antibody compositions for selectively inhibiting VEGF  
INVENTOR(S): Thorpe, Philip E., Dallas, TX, United States  
Brekken, Rolf A., Seattle, WA, United States  
PATENT ASSIGNEE(S): Board of Regents, The University of Texas System,  
Austin, TX, United States (U.S. corporation)

|                     | NUMBER         | KIND | DATE         |
|---------------------|----------------|------|--------------|
| PATENT INFORMATION: | US 6342219     | B1   | 20020129     |
| APPLICATION INFO.:  | US 2000-561500 |      | 20000428 (9) |

|                       | NUMBER                                 | DATE          |
|-----------------------|--|---------------|
| PRIORITY INFORMATION: | US 1999-131432P                        | 19990428 (60) |
| DOCUMENT TYPE:        | Utility                                |               |
| FILE SEGMENT:         | GRANTED                                |               |
| PRIMARY EXAMINER:     | Chan, Christina Y.                     |               |
| ASSISTANT EXAMINER:   | Huynh, Phuong N.                       |               |
| LEGAL REPRESENTATIVE: | Williams, Morgan and Amerson           |               |
| NUMBER OF CLAIMS:     | 50                                     |               |
| EXEMPLARY CLAIM:      | 20                                     |               |
| NUMBER OF DRAWINGS:   | 7 Drawing Figure(s); 4 Drawing Page(s) |               |
| LINE COUNT:           | 10403                                  |               |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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DETD . . . decrease the severity of symptoms; decrease the duration of disease exacerbations; increase the frequency and duration of disease remission/symptom-free periods; **prevent** fixed impairment and disability; and/or **prevent**/attenuate chronic progression of the disease. Clinically, this would result in improvement in visual symptoms (visual loss, diplopia), gait disorders (weakness, . . . dysfunction (weakness, spasticity, sensory loss), bladder dysfunction (urgency, incontinence, hesitancy, incomplete emptying), depression, emotional lability, and cognitive impairment. Pathologically the **treatment reduces** one or more of the following, such as myelin loss, breakdown of the blood-brain barrier, perivascular infiltration of mononuclear cells, immunologic abnormalities, gliotic **scar** formation and astrocyte proliferation, metalloproteinase production, and impaired conduction velocity.

DETD . . . Utilizing the agents, compositions and methods provided herein a wide variety of surgical adhesions and complications of surgery can be **treated** or **prevented**. Adhesion formation or unwanted **scar** tissue accumulation/encapsulation complicates a variety of surgical procedures. As described above, surgical adhesions complicate virtually any open or endoscopic surgical. . . the function of the surgical implant (e.g., breast implant, artificial joint, surgical mesh, vascular graft, dural patch). Chronic inflammation and **scarring** also occurs during surgery to correct chronic sinusitis or removal of other regions of chronic inflammation (e.g., foreign bodies, infections.

DETD . . . "film", or "wrap" which releases the drug over a period of time such that the incidence of surgical adhesions is **reduced**. During endoscopic procedures, the paclitaxel-polymer preparation is applied as a "spray", via delivery ports in the endoscope, to the mesentery. . . to 20% paclitaxel is applied to the surface of the surgical implant (e.g., breast implant, artificial joint, vascular graft) to **prevent** encapsulation/inappropriate **scarring** in the vicinity of the implant. In yet another preferred embodiment, a polymeric implant containing 0.1% to 20% paclitaxel by. . . cavity, chest cavity, abdominal cavity, or at the operative site during neurosurgery) such that recurrence of inflammation, adhesion formation, or **scarring** is **reduced**. In another embodiment, lavage fluid containing 1 to 75 mg/m.sup.2 (preferably 10 to 50 mg/m.sup.2) paclitaxel, would be used at. . .

|                           |                    |     |             |
|---------------------------|--------------------|-----|-------------|
| DETD                      | . . . paste (3 mg) | 20% | 0/10        |
| MDHC (tyrosine inhibitor) | PCL paste (3 mg)   | 20% | 0/8         |
| erbstatin                 | PCL paste (3 mg)   | 20% | 0/5         |
|                           |                    |     | - too toxic |
| genistein                 | PCL paste (3 mg)   | 10% | 0/7         |
|                           | PCL paste (3 mg)   | 20% | 0/4         |
| herbimysin                | PCL paste (3 mg)   | 2%  | 3/4         |
|                           | PCL paste. . .     |     |             |

DETD . . . polymer or a 2 mm thick disc of polymer, either of which may be applied to the tissue surface to **prevent** subsequent **scarring** and adhesion formation. This film was designed to be placed on exposed tissue so that any encapsulated drug can be. . .

ACCESSION NUMBER: 2002:22462 USPATFULL  
TITLE: COMPOSITIONS AND METHODS FOR TREATING OR PREVENTING INFLAMMATORY DISEASES  
INVENTOR(S): HUNTER, WILLIAM L., VANCOUVER, CANADA

|                       | NUMBER   | KIND  | DATE         |
|-----------------------|--|-------|--------------|
|                       | -----  | ----- | -----        |
| PATENT INFORMATION:   | US 2002013298                                      | A1    | 20020131     |
| APPLICATION INFO.:    | US 1999-368463                                     | A1    | 19990804 (9) |
| RELATED APPLN. INFO.: | Division of Ser. No. US 1998-88546, filed on 1 Jun |       |              |

1998, PENDING Continuation-in-part of Ser. No. US  
1997-980549, filed on 1 Dec 1997, PENDING

|  | NUMBER   | DATE          |
|--|--|---------------|
| PRIORITY INFORMATION:                      | US 1996-32215P   | 19961202 (60) |
|  | US 1997-63087P   | 19971024 (60) |
| DOCUMENT TYPE:                             | Utility  |               |
| FILE SEGMENT:                              | APPLICATION  |               |
| LEGAL REPRESENTATIVE:                      | SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH<br>AVE, SUITE 6300, SEATTLE, WA, 98104-7092 |               |
| NUMBER OF CLAIMS:                          | 45   |               |
| EXEMPLARY CLAIM:                           | 1  |               |
| NUMBER OF DRAWINGS:                        | 110 Drawing Page(s)  |               |
| LINE COUNT:                                | 8318   |               |
| CAS INDEXING IS AVAILABLE FOR THIS PATENT. |  |               |

L36 ANSWER 47 OF 149 USPATFULL on STN

SUMM . . . harmless topical depigmenting substances with good efficacy.  
The use of such substances with good efficacy is most particularly  
desired for **treating** regional hyperpigmentations caused by  
melanocyte hyperactivity, such as idiopathic melasmas, occurring during  
pregnancy ("pregnancy mask" or chloasma) or during oestro-progestative.  
. . . post-lesional cicatrization, and also certain leukodermas, such as  
vitiligo. For these conditions (in which the cicatrizations can result  
in a **scar** which gives the skin a whiter appearance) and for  
leukodermas, failing the ability to repigment the damage to skin, the.

DETD [0040] Isoflavonoids of natural origin are preferably used. Included  
are: daidzin, genistin, daidzein, formononetin, cuneatin,  
**genistein**, isopruneitin and prunetin, cajanin, orobol,  
pratensein, santal, junipegein A, glycitein, afrormosin, retusin,  
tectorigenin, irisolidone, and jamaicin, and also analogues and. . .

DETD [0041] Isoflavones are preferred for use in the present invention. This  
term covers both the aglycone forms (e.g., daidzein, **genistein**  
and glycitein) and the glycosylated forms (e.g., daidzine, genistine,  
glycitine) of the isoflavones.

CLM What is claimed is:

. . . composition according to claim 1, wherein said isoflavonoid is  
selected from the group consisting of daidzin, genistin, daidzein,  
formononetin, cuneatin, **genistein**, isopruneitin and prunetin,  
cajanin, orobol, pratensein, santal, junipegein A, glycitein,  
afrormosin, retusin, tectorigenin, irisolidone, jamaicin, and mixtures  
thereof.

IT 446-72-0, Genistein 480-23-9, Orobol 485-72-3, Formononetin  
486-66-8, Daidzein 529-59-9, Genistin 529-60-2, Santal 548-77-6,  
Tectorigenin 550-79-8, Afrormosin 552-59-0, Prunetin 552-66-9,  
Daidzin 2284-31-3, Pratensein 2345-17-7, Irisolidone 4569-98-6,  
Isopruneitin 7159-95-7 7741-28-8, Cuneatin 21572-58-7 24211-36-7,  
Jamaicin 32884-36-9, Cajanin 37816-19-6, Retusin 40957-83-3,  
Glycitein 54734-40-6 76265-28-6, Junipegein a 220717-78-2  
(skin whitening cosmetic compns. comprising aminophenol derivative and  
isoflavonoid)

ACCESSION NUMBER: 2002:199172 USPATFULL  
TITLE: Cosmetic composition containing an aminophenol  
derivative and an isoflavonoid  
INVENTOR(S): Chevalier, Veronique, Villecresnes, FRANCE  
Pham, Dang-Man, Sucy-En-Brie, FRANCE  
PATENT ASSIGNEE(S): L'OREAL, Paris, FRANCE (non-U.S. corporation)

|                     | NUMBER         | KIND | DATE         |
|---------------------|----------------|------|--------------|
| PATENT INFORMATION: | US 2002107282  | A1   | 20020808     |
| APPLICATION INFO.:  | US 2001-986885 | A1   | 20011113 (9) |

|                       | NUMBER  | DATE     |
|-----------------------|---|----------|
| PRIORITY INFORMATION: | FR 2000-14479   | 20001110 |
| DOCUMENT TYPE:        | Utility   |          |
| FILE SEGMENT:         | APPLICATION   |          |
| LEGAL REPRESENTATIVE: | OBLON SPIVAK MCCLELLAND MAIER & NEUSTADT PC, FOURTH<br>FLOOR, 1755 JEFFERSON DAVIS HIGHWAY, ARLINGTON, VA,<br>22202 |          |
| NUMBER OF CLAIMS:     | 20  |          |
| EXEMPLARY CLAIM:      | 1   |          |

L36 ANSWER 41 OF 149 USPATFULL on STN

SUMM [0012] U.S. Pat. No. 6,228,887 to Kligman discloses **treating** such skin disorders as photodamage, hyperpigmentation, rosacea, and **scarring** topically with high strength retinoids at a concentration effective to cause desquamation. Retinoids activate the the epidermal growth factor receptor, . . . skin cells, which results in the desquamation sought by this patent. The clinical examples given in this patent only involve **treating** photodamaged skin.

DETD [0018] The art has addressed inflammation and **scarring** caused by acne as a secondary benefit to the **treatment** of the disease; that is, if the acne is cured the factors causing **scarring** will be eliminated. There is otherwise no **treatment** directed at **preventing scarring** from acne. Neither is there presently any direct **treatment** for the inflammation accompanying acne. The conventional **treatment** acts to **prevent** further problems by alleviating the cause of the acne; for example, a patient is **treated** with tetracycline, an antibiotic, in hopes of killing the P. acnes, and the death of the bacteria will effectively end the inflammation and future **scarring**. Much as antipyretics, analgesics, decongestants, and antihistamines have been developed to **treat** the symptoms of colds and upper respiratory infections (as opposed to antibiotics and antivirals to kill off the invading bacteria and viruses), there is a need for **treatments** diminishing if not **preventing scarring** and inflammation in acne.

DETD . . . areas of injury, invade acne-affected skin, and release both a collagenase (MMP-8) and another protease (neutrophil elastase) that likely exacerbate **scarring**. Additionally, we have discovered that acne-affected skin has an elevated collagenase (MMP-1) level from resident skin cells that further exacerbates **scarring**. We have disclosed that **inhibition** of these dermal matrix-degrading enzymes with the use of MMP **inhibitors** (in addition to and including retinoids) can **lessen scarring** of acne-affected skin. Neutrophils circulate in the blood and therefore must be recruited by a signalling mechanism to induce their. . .

DETD [0029] Indirect MMP inhibitors include the kinase inhibitors **genistein** and quercetin (as described in U.S. Pat. No. 5,637,703, U.S. Pat. No. 5,665,367, and FR-A-2,671,724, and related compounds, as well. . .

DETD . . . inhibits proliferation, and induces apoptosis of acute myelogenous leukemia cells", Blood, vol. 94, no. 8, Oct. 15, 1999 (pp. 2844-53). **Genistein**: Tabary et al., "Genistein inhibits constitutive and inducible NFkappaB activation and decreases IL-8 production by human cystic fibrosis bronchial gland cells", Am J. Pathol., . . . 12-epi-scalaradial, and LY311727; arachidonyl methyl ketone analogue (AACOH.sub.3) and the eicosapentanoyl analogue (EPACHOHCF.sub.3) had no effect on TNF-induced NF-kB activation. **Genistein**, erbstatin: Natarajan et al., "Protein tyrosine kinase inhibitors block tumor necrosis factor-induced activation of nuclear factor-KB, degradation of IKB $\alpha$ , nuclear. . .

DETD [0033] **Inhibitors** of TLRs (toll-like receptors) and/or other receptors that are sensitive to the LPS-like compounds associated with **acne lesions** can be used to ameliorate the signalling that induces the cytokines TNF $\alpha$ , IL-1 $\beta$ , IL-8, and IL-10, as shown in. . .

ACCESSION NUMBER: 2002:323230 USPATFULL  
TITLE: Method and compositions for treating rosacea  
INVENTOR(S): Kang, Sewon, Ann Arbor, MI, UNITED STATES  
Voorhees, John J., Ann Arbor, MI, UNITED STATES  
Fisher, Gary J., Ypsilanti, MI, UNITED STATES

| NUMBER | KIND  | DATE  |
|--------|-------|-------|
| -----  | ----- | ----- |

PATENT INFORMATION: US 2002183399 A1 20021205  
APPLICATION INFO.: US 2002-142724 A1 20020509 (10)

|                       | NUMBER  | DATE          |
|-----------------------|---|---------------|
| PRIORITY INFORMATION: | US 2001-289758P   | 20010509 (60) |
| DOCUMENT TYPE:        | Utility   |               |
| FILE SEGMENT:         | APPLICATION   |               |
| LEGAL REPRESENTATIVE: | Bradley N. Ruben, Suite 5A, 463 First Street, Hoboken,<br>NJ, 07030 |               |
| NUMBER OF CLAIMS:     | 18  |               |
| EXEMPLARY CLAIM:      | 1   |               |
| LINE COUNT:           | 896   |               |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . been shown to inhibit apoptosis in cerebellar granule cells, although by distinct mechanisms (Galli et al., 1995). The protein tyrosine kinase inhibitors **genistein** and herbimycin A have both been shown to prevent anti-CD3 monoclonal antibody-induced thymic apoptosis (Migita et al., 1994). Interleukin-6 (IL-6) inhibits constitutive, . . . vivo. Inducing or speeding up the overall regeneration process by administering regenerated tissue to the site of injury is beneficial as it **lessens** the chance that the body will attempt to repair the injury, leading to the formation of **scar** tissue and the loss of normal tissue structure and function.

ACCESSION NUMBER: 1997045533 PCTFULL ED 20020514  
 TITLE (ENGLISH): ENGINEERING ORAL TISSUES  
 TITLE (FRENCH): RECONSTITUTION DE TISSUS BUCCAUX  
 INVENTOR(S): MOONEY, David, J.;  
 RUTHERFORD, Robert, Bruce  
 PATENT ASSIGNEE(S): THE REGENTS OF THE UNIVERSITY OF MICHIGAN;  
 MOONEY, David, J.;  
 RUTHERFORD, Robert, Bruce  
 LANGUAGE OF PUBL.: English  
 DOCUMENT TYPE: Patent  
 PATENT INFORMATION:

| NUMBER     | KIND | DATE     |
|------------|------|----------|
| WO 9745533 | A1   | 19971204 |

DESIGNATED STATES  
 W:

AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE  
 ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS  
 LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG  
 SI SK TJ TM TR TT UA UG US UZ VN YU GH KE LS MW SD SZ  
 UG AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR  
 GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML  
 MR NE SN TD TG

APPLICATION INFO.: WO 1997-US8977 A 19970528  
 PRIORITY INFO.: US 1996-60/018,450 19960528



L36 ANSWER 149 OF 149 SCISEARCH COPYRIGHT 2004 FOUNDED BY  
 AN 96:891798 SCISEARCH  
 GA The Genuine Article (R) Number: VV058  
 TI Integrin alpha 2 beta 1-dependent contraction of floating collagen gels  
 and induction of collagenase are inhibited by tyrosine kinase inhibitors  
 AU Broberg A; Heino J (Reprint)  
 CS UNIV TURKU, MEDICITY RES LAB, FIN-20520 TURKU, FINLAND (Reprint); UNIV  
 TURKU, MEDICITY RES LAB, FIN-20520 TURKU, FINLAND; UNIV TURKU, DEPT  
 BIOCHEM MED, FIN-20520 TURKU, FINLAND  
 CYA FINLAND  
 SO EXPERIMENTAL CELL RESEARCH, (10 OCT 1996) Vol. 228, No. 1, pp. 29-35.  
 Publisher: ACADEMIC PRESS INC JNL-COMP SUBSCRIPTIONS, 525 B ST, STE 1900,  
 SAN DIEGO, CA 92101-4495.  
 ISSN: 0014-4827.  
 DT Article; Journal  
 FS LIFE  
 LA English  
 REC Reference Count: 39  
 AB A cell culture inside a three-dimensional gel of fibrillar collagen is  
 an experimental model used to study the response of cells to the  
 extracellular matrix. Many cell types induce the contraction of gel and  
 simultaneously decrease their production of type I collagen, whereas the  
 expression of interstitial collagenase (matrix metalloproteinase-1; MMP-1)  
 is enhanced. We have previously shown that in osteogenic cells the  
 collagen receptor alpha 2 beta 1 integrin is a positive regulator of MMP-1  
 and that the number of alpha 2 beta 1 integrins on the cell surface also  
 regulates the magnitude of contraction. However, the downregulation of  
 collagen mRNA levels is not initiated by alpha 2 beta 1 integrin. Here, we  
 have studied in human KHOS-240 and MG-63 osteosarcoma cells and in human  
 skin fibroblasts the effects of tyrosine kinase inhibitors on collagen gel  
 contraction and on the regulation of MMP-1 and collagen alpha 1(I) genes  
 by extracellular collagen. The induction of MMP-1 could be inhibited by  
 all tyrosine kinase inhibitors tested with the exception of  
**genistein**. None of them could prevent the downregulation of  
 collagen expression. Thus, the collagen-induced alterations in the  
 expression of MMP-1 and collagen alpha 1(I) seem to be dependent on  
 distinct signal transduction pathways. Many of the **inhibitors**,  
 including **genistein**, could **prevent** the contraction of  
 collagen gels. The effect was not related to their ability to  
**inhibit** cell growth, because an **inhibitor** specific for  
 DNA synthesis and cell division did not have the same effect. Thus, we  
 suggest that the process of collagen gel contraction requires  
 protein-tyrosine phosphorylation and that the ability of cells to contract  
 collagen gels is not related to the induction of MMP-1 or to the level of  
 collagen alpha 1(I) expression. Finally, we propose that the tyrosine  
 kinase **inhibitors** might be considered as candidate molecules in  
 the **treatment** of pathological **scar** contraction. (C)  
 1996 Academic Press, Inc.  
 CC ONCOLOGY; CELL BIOLOGY  
 STP KeyWords Plus (R): GENE-EXPRESSION; SIGNAL-TRANSDUCTION; LATTICE  
 CONTRACTION; FIBROBLASTS; RECEPTOR; BINDING; PROTEIN; SUBUNIT; DOMAIN;  
 CELLS  
 RF 94-0081 002; NADPH OXIDASE ACTIVATION; SMALL GTP-BINDING PROTEINS; CHRONIC  
 GRANULOMATOUS-DISEASE  
 94-0484 002; ADHESION MOLECULES; P-SELECTIN GLYCOPROTEIN LIGAND; LEUKOCYTE  
 HOMING RECEPTORS  
 94-0971 001; MATRIX METALLOPROTEINASE EXPRESSION; TISSUE INHIBITOR; 92-KD  
 TYPE-IV COLLAGENASE ACTIVITY; CULTURED VASCULAR SMOOTH-MUSCLE CELLS;  
 PLASMINOGEN ACTIVATION  
 94-2201 001; COLLAGEN GEL CONTRACTION; FIBROBLASTS IN-VITRO; TRANSFORMING  
 GROWTH-FACTOR-BETA  
 RE  
 Referenced Author | Year | VOL | PG | Referenced Work

| (RAU)             | (RPY) | (RVL) | (RPG) | (RWK)                |
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| GULLBERG D        | 1992  | 11    | 3865  | EMBO J               |
| GULLBERG D        | 1990  | 186   | 264   | EXP CELL RES         |
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| HUHTALA P         | 1995  | 129   | 867   | J CELL BIOL          |
| HYNES R O         | 1992  | 69    | 11    | CELL                 |
| KATAMA T          | 1994  | 269   | 9659  | J BIOL CHEM          |
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| LEE J O           | 1995  | 80    | 631   | CELL                 |
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| RIIKONEN T        | 1995  | 270   | 13548 | J BIOL CHEM          |
| RUOSLAHTI E       | 1991  | 87    | 1     | J CLIN INVEST        |
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| TREMBLE P         | 1995  | 129   | 1707  | J CELL BIOL          |
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| WERB Z            | 1989  | 109   | 877   | J CELL BIOL          |
| YAMATO M          | 1995  | 117   | 940   | J BIOCHEM-TOKYO      |

=>

SUMM Anti-acne actives can be effective in **treating** acne vulgaris, a chronic disorder of the pilosebaceous follicles. The condition involves inflammation of the pilosebaceous apparatus thereby resulting in lesions, which may include papules, pustules, cysts, comedones, and severe **scarring**. The bacteria *Corynebacterium acnes* and *Staphylococcus epidermidis* are usually present in the pustular contents.

SUMM Anti-wrinkle, anti-skin atrophy and skin repair actives can be effective in replenishing or rejuvenating the epidermal layer. These actives generally provide these desirable skin care benefits by promoting or maintaining the natural process of desquamation. Nonlimiting examples of antiwrinkle and anti-skin atrophy actives include retinoic acid and its derivatives (e.g., cis and trans); retinal; retinol; retinyl esters such as retinyl acetate, retinyl palmitate, and retinyl propionate; vitamin B.sub.3 compounds (such as niacinamide and nicotinic acid), salicylic acid and derivatives thereof (such as 5-octanoyl salicylic acid, heptyloxy 4 salicylic acid, and 4-methoxy salicylic acid); sulfur-containing D and L amino acids and their derivatives and salts, particularly the N-acetyl derivatives, a preferred example of which is N-acetyl-L-cysteine; thiols, e.g. ethane thiol; hydroxy acids, phytic acid, lipoic acid; lysophosphatidic acid; skin peel agents (e.g., phenol and the like); Actein 27-Deoxyactein Cimicifugoside (available from Cirmigoside); adapalene; ademethionine; adenosine; aletris extract; alkyl glutathione esters; alkoxyalkoxy alkoxyn benzoic and derivatives; aloe derived lectins; amino propane phosphoric acid; 3-aminopropyl dihydrogen phosphate; Amadorine (available from Barnet Products); anise extracts; AOSINE (available from Secma); arginine amino benzoate; ASC III (available from E. Merck, located in Darmstadt, Germany); ascorbic acid; ascorbyl palmitate; asiatic acid; asiaticosides; ARLAMOL GEO.TM. (available from ICI, located in Wilmington, Del.); azaleic acid; benzoic acid derivatives; bertholletia extracts; betulinic acid; BIOCHANIN A AND BIOPEPTIDE CL (available from Sederma, located in Brooklyn, N.Y.); BIOPEPTIDE EL (available from Sederma); biotin; blackberry bark extract; blackberry lily extracts; black cohosh extract; blue cohosh extract; butanoyl betulinic acid; carboxymethyl 1,3 beta glucan; catecholamines; chalcones; citric acid esters; chaste tree extract; clover extracts; coumestrol; CPC Peptide (available from Barnet Products); daidzein; dang gui extract; darutoside; debromo laurinterol; 1-decanoyl-glycero-phosphonic acid; dehydrocholesterol; dehydrodicreosol; dehydrodieugenol; dehydroepiandrosterone; DERMOLECTINE (available from Sederma); dehydroascorbic acid; dehydroepiandrosterone sulfate; dianethole; dihydroxy benzoic acid; 2,4 dihydroxybenzoic acid; diglycol guanidine succinate; diosgenin; disodium ascorbyl phosphate; dodecanedioic acid; Ederline (available from Seporga); Enderline (available from Laboratories Seporga); equol; eriodictyol; estrogen and its derivatives; ETF (available from Laboratories Seporga); ethocyn; ELESERYL SH (available from Laboratories Serobiologiques, located in Somerville, N.J.); ENDONUCLEINE (available from Laboratories Serobiologiques); ergosterol; eythrobic acid; fennel extract; fenugreek seed extract; FIBRASTIL (available from Sederma); FIBROSTIMULINES S and P (available from Sederma); FIRMOGEN LS 8445 (available from Laboratories Serobiologiques); formononetin; forsythia fruit extract; gallic acid esters; gamma amino butyric acid; GATULINE RC (available from Gattlefosse, located in Priest, France); **genistein**; genisteine; genistic acid; gentisyl alcohol; ginkgo bilboa extracts; ginseng extracts; ginsenoside (RO, R.sub.6-1, R.sub.6-2, R.sub.6-3, R.sub.C, R.sub.D, R.sub.E, R.sub.F, R.sub.F-2, R.sub.G-1, R.sub.G-2); gluco pyranosyl-L-ascorbate; glutathione and its esters; glycitein; hesperitin; hexahydro curcumin; HMG- coenzyme A reductase inhibitors; hops extracts; 11 hydroxy undecanoic acid; 10 hydroxy decanoic acid; 25-hydroxycholesterol; 7-hydroxylated sterols; hydroxyethyl isostearyloxy isopropanolamine; hydroxy-tetra methyl piperidinyloxy;

hypotaurine; ibukijakou extract; isoflavone SG 10 (available from Barnet Products); kinetin; kohki extract; L-2-OXO-thiazolidine-4-carboxylic acid esters; lactate dehydrogenase inhibitors; 1-lauryl, -lyso-phosphatidyl choline; lectins; lichochalcone LF15 (available from Maruzen); licorice extracts; lignan; lumisterol; lupenes; luteolin; lysophosphitidic acid; magnesium ascorbyl phosphate; margin; melatonin; melibiose; metalloproteinase inhibitors; methoprene; methoprenic acid; mevalonic acid; MPC COMPLEX (available from CLR); N methyl serine; N methyl taurine; N, N.sup.1-bis (lactyl) cysteamine; naringenin; neotigogenin; o-desmethylangoiensin; oat beta glucan; oleanolic acid; pantethine; phenylalanine; photoanethone; piperidine; placental extracts; pratensein; pregnenolone; pregnenolone acetate; pregnenolone succinate; premarin; quillaic acid; raloxifene; REPAIR FACTOR 1 and REPAIR FACTOR FCP (both available from Sederna); retinoates (esters of C.sub.2-C.sub.20 alcohols); retinyl glucuronate; retinyl linoleate; S-carboxymethyl cysteine; SEANAMINE FP (available from Laboratories Serobiologiques); sodium ascorbyl phosphate; soya extracts; spleen extracts; tachysterol; taurine; tazarotene; tempol; thymulen; thymus extracts; thyroid hormones; tigogenin; tocopheryl retinoate; toxifolin; traumatic acid; tricholine citrate; trifoside; uracil derivatives; ursolic acid; vitamin D.sub.3 and its analogs; vitamin K; vitex extract; yam extract; yamogenin; zeatin; and mixtures thereof.

ACCESSION NUMBER: 2002:9654 USPATFULL  
 TITLE: Cleansing articles for skin and/or hair which also deposit skin care actives  
 INVENTOR(S): Albacarys, Lourdes Dessus, West Chester, OH, United States  
 McAtee, David Michael, Mason, OH, United States  
 Deckner, George Endel, Cincinnati, OH, United States  
 PATENT ASSIGNEE(S): The Procter & Gamble Company, Cincinnati, OH, United States (U.S. corporation)

|                       | NUMBER   | KIND | DATE         |
|-----------------------|--|------|--------------|
| PATENT INFORMATION:   | US 6338855   | B1   | 20020115     |
| APPLICATION INFO.:    | US 1999-296334   |      | 19990422 (9) |
| RELATED APPLN. INFO.: | Continuation-in-part of Ser. No. US 1998-65991, filed on 24 Apr 1998, now abandoned Continuation-in-part of Ser. No. US 1997-974033, filed on 19 Nov 1997, now abandoned Continuation-in-part of Ser. No. US 1996-738145, filed on 25 Oct 1996, now abandoned Continuation of Ser. No. US 1996-738668, filed on 25 Oct 1996, now abandoned |      |              |

|  | NUMBER   | DATE          |
|--|--|---------------|
| PRIORITY INFORMATION:                      | US 1998-83015P   | 19980424 (60) |
| DOCUMENT TYPE:                             | Utility  |               |
| FILE SEGMENT:                              | GRANTED  |               |
| PRIMARY EXAMINER:                          | Criares, Theodore J.                                   |               |
| LEGAL REPRESENTATIVE:                      | Allen, George W., Matthews, Armina E., Tsuneki, Fumiko |               |
| NUMBER OF CLAIMS:                          | 29   |               |
| EXEMPLARY CLAIM:                           | 1  |               |
| NUMBER OF DRAWINGS:                        | 0 Drawing Figure(s); 0 Drawing Page(s)                 |               |
| LINE COUNT:                                | 3405   |               |
| CAS INDEXING IS AVAILABLE FOR THIS PATENT. |  |               |

L36 ANSWER 68 OF 149 USPATFULL on STN

DETD . . . to inhibit apoptosis in cerebellar granule cells, although by distinct mechanisms (Galli et al., 1995). The protein tyrosine kinase inhibitors **genistein** and herbimycin A have both been shown to prevent anti-CD3 monoclonal antibody-induced thymic apoptosis (Migita et al., 1994). Interleukin-6 (IL-6). . .

DETD . . . or speeding up the overall regeneration process by administering regenerated tissue to the site of injury is beneficial as it **lessens** the chance that the body will attempt to repair the injury, leading to the formation of **scar** tissue and the loss of normal tissue structure and function.

PI US 5885829 19990323

LL on STN

DETD . . . inflammatory diseases including but not limited to rheumatoid arthritis, inflammatory bowel disease, multiple sclerosis, psoriasis and asthma; wound healing and **scar reduction**; and neurodegenerative diseases. Therefore, the development of cell-based assays that provide information on the effect of a test compound on. .

DETD . . . of tumor growth and metastasis, angiogenesis, thrombosis, restenosis, vascular overgrowth during macular degeneration, foam cell formation, inflammatory diseases, wound healing, **scar reduction**, and neurodegenerative diseases.

DETD . . . 10  $\mu$ M Calphostin C (a protein kinase C inhibitor), 10  $\mu$ M KN-52 (a Calmodulin dependent protein kinase inhibitor), 10  $\mu$ M **genistein** (a tyrosine kinase inhibitor) and 10 nM wortmannin (a phosphatidyl inositol kinase inhibitor). These agents were also applied during measurement. . . different from the profile for cell motility. Calphostin C, for example, was equally effective at inhibiting cell spreading and movement, **genistein** and KN-62 were ineffective at the concentrations used at blocking either cellular response, and Wortmannin was more effective at blocking. . .

CLM What is claimed is:

. . . of tumor growth and metastasis, angiogenesis, thrombosis, restenosis, vascular overgrowth during macular degeneration, foam cell formation, inflammatory diseases, wound healing, **scar reduction**, and neurodegenerative diseases.

. . . of tumor growth and metastasis, angiogenesis, thrombosis, restenosis, vascular overgrowth during macular degeneration, foam cell formation, inflammatory diseases, wound healing, **scar reduction**, and neurodegenerative diseases.

. . . of tumor growth and metastasis, angiogenesis, thrombosis, restenosis, vascular overgrowth during macular degeneration, foam cell formation, inflammatory diseases, wound healing, **scar reduction**, and neurodegenerative diseases.

PI US 2001041347 A1 20011115|  
US 6716588 B2 20040406|

LL on STN

DETD . . . inflammatory diseases including but not limited to rheumatoid arthritis, inflammatory bowel disease, multiple sclerosis, psoriasis and asthma; wound healing and **scar reduction**; and neurodegenerative diseases. Therefore, the development of cell-based assays that provide information on the effect of a test compound on. .

DETD . . . of tumor growth and metastasis, angiogenesis, thrombosis, restenosis, vascular overgrowth during macular degeneration, foam cell formation, inflammatory diseases, wound healing, **scar reduction**, and neurodegenerative diseases.

DETD . . . 10  $\mu$ M Calphostin C (a protein kinase C inhibitor), 10  $\mu$ M KN-52 (a Calmodulin dependent protein kinase inhibitor), 10  $\mu$ M **genistein** (a tyrosine kinase inhibitor) and 10 nM wortmannin (a phosphatidyl inositol kinase inhibitor). These agents were also applied during measurement. . . different from the profile for cell motility. Calphostin C, for example, was equally effective at inhibiting cell spreading and movement, **genistein** and KN-62 were ineffective at the concentrations used at blocking either cellular response, and Wortmannin was more effective at blocking. . .

CLM What is claimed is:

. . . of tumor growth and metastasis, angiogenesis, thrombosis, restenosis, vascular overgrowth during macular degeneration, foam cell formation, inflammatory diseases, wound healing, **scar reduction**, and neurodegenerative diseases.

. . . of tumor growth and metastasis, angiogenesis, thrombosis, restenosis, vascular overgrowth during macular degeneration, foam cell formation, inflammatory diseases, wound healing, **scar reduction**, and neurodegenerative diseases.

. . . of tumor growth and metastasis, angiogenesis, thrombosis, restenosis, vascular overgrowth during macular degeneration, foam cell formation, inflammatory diseases, wound healing, **scar reduction**, and neurodegenerative diseases.

PI US 2001041347 A1 20011115|  
US 6716588 B2 20040406|

L28 ANSWER 12 OF 14 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

AN 96321992 EMBASE

DN 1996321992

TI Integrin  $\alpha 2 \beta 1$ -dependent contraction of floating collagen gels  
and induction of collagenase are inhibited by tyrosine kinase inhibitors.

AU Broberg A.; Heino J.

CS Department of Medical Biochemistry, MediCity Research Laboratory,  
University of Turku, Tykistokatu 6A, FIN-20520 Turku, Finland

SO Experimental Cell Research, (1996) 228/1 (29-35).  
ISSN: 0014-4827 CODEN: ECREAL

CY United States

DT Journal; Article

FS 029 Clinical Biochemistry

LA English

SL English

AB A cell culture inside a three-dimensional gel of fibrillar collagen is an  
experimental model used to study the response of cells to the  
extracellular matrix. Many cell types induce the contraction of gel and  
simultaneously decrease their production of type I collagen, whereas the  
expression of interstitial collagenase (matrix metalloproteinase-1; MMP-1)  
is enhanced. We have previously shown that in osteogenic cells the  
collagen receptor  $\alpha 2 \beta 1$  integrin is a positive regulator of  
MMP-1 and that the number of  $\alpha 2 \beta 1$  integrins on the cell surface  
also regulates the magnitude of contraction. However, the downregulation  
of collagen mRNA levels is not initiated by  $\alpha 2 \beta 1$  integrin.  
Here, we have studied in human KHOS-240 and MG- 63 osteosarcoma cells and  
in human skin fibroblasts the effects of tyrosine kinase inhibitors on  
collagen gel contraction and on the regulation of MMP-1 and collagen  
 $\alpha 1(I)$  genes by extracellular collagen. The induction of MMP-1 could  
be inhibited by all tyrosine kinase inhibitors tested with the exception  
of **genistein**. None of them could prevent the downregulation of  
collagen expression. Thus, the collagen-induced alterations in the  
expression of MMP-1 and collagen  $\alpha 1(I)$  seem to be dependent on  
distinct signal transduction pathways. Many of the inhibitors, including  
**genistein**, could prevent the contraction of collagen gels. The  
effect was not related to their ability to inhibit cell growth, because an  
inhibitor specific for DNA synthesis and cell division did not have the  
same effect. Thus, we suggest that the process of collagen gel contraction  
requires protein-tyrosine phosphorylation and that the ability of cells to  
contract collagen gels is not related to the induction of MMP-1 or to the  
level of collagen  $\alpha 1(I)$  expression. Finally, we propose that the  
tyrosine kinase inhibitors might be considered as candidate molecules in  
the treatment of pathological **scar** contraction.

CT Medical Descriptors:  
\*extracellular matrix  
article  
collagen synthesis  
controlled study  
enzyme induction  
enzyme phosphorylation  
human  
human cell  
priority journal  
protein expression  
Drug Descriptors:  
\*collagen gel  
\*collagenase: EC, endogenous compound  
\*integrin  
\*protein tyrosine kinase inhibitor  
collagen type 1  
RN (collagenase) 9001-12-1



L7 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1996:746408 CAPLUS  
 DN 126:14769  
 ED Entered STN: 20 Dec 1996  
 TI Pharmaceutical composition containing substance inhibiting HSP47  
 production  
 IN Kiyosuke, Yoichi; Shirakami, Toshiharu; Morino, Masayoshi; Yoshikumi,  
 Chikao  
 PA Kureha Chemical Industry Co., Ltd., Japan  
 SO Eur. Pat. Appl., 23 pp.  
 CODEN: EPXXDW  
 DT Patent  
 LA English  
 IC ICM A61K035-78  
 ICS A61K031-35; A61K031-70; A61K035-84; A61K038-00; A61K031-355;  
 A61K031-19  
 CC 1-10 (Pharmacology)  
 FAN.CNT 1

|    | PATENT NO. | KIND | DATE     | APPLICATION NO. | DATE     |
|----|------------|------|----------|-----------------|----------|
| PI | EP 742012  | A2   | 19961113 | EP 1996-107224  | 19960508 |
|    | EP 742012  | A3   | 19990908 |                 |          |

R: DE, FR, GB, NL

|      |                |    |          |                 |          |
|------|----------------|----|----------|-----------------|----------|
|      | JP 08301757    | A2 | 19961119 | JP 1995-136028  | 19950510 |
|      | JP 08301784    | A2 | 19961119 | JP 1995-136029  | 19950510 |
|      | JP 2892300     | B2 | 19990517 |                 |          |
|      | JP 09012459    | A2 | 19970114 | JP 1995-186302  | 19950629 |
|      | JP 3003978     | B2 | 20000131 |                 |          |
|      | JP 09040556    | A2 | 19970210 | JP 1995-210935  | 19950727 |
|      | JP 09040553    | A2 | 19970210 | JP 1995-211274  | 19950728 |
|      | JP 2933511     | B2 | 19990816 |                 |          |
|      | CA 2175985     | AA | 19961111 | CA 1996-2175985 | 19960507 |
|      | AU 9652140     | A1 | 19961219 | AU 1996-52140   | 19960507 |
|      | AU 689036      | B2 | 19980319 |                 |          |
| PRAI | JP 1995-136027 | A  | 19950510 |                 |          |
|      | JP 1995-136028 | A  | 19950510 |                 |          |
|      | JP 1995-136029 | A  | 19950510 |                 |          |
|      | JP 1995-186302 | A  | 19950629 |                 |          |
|      | JP 1995-210935 | A  | 19950727 |                 |          |
|      | JP 1995-211274 | A  | 19950728 |                 |          |

AB A pharmaceutical composition for treatment of liver cirrhosis, interstitial  
 lung disease, chronic renal failure, **scars**, scleroderma,  
 arteriosclerosis, and rheumatoid arthritis contains a substance which  
 inhibits HSP47 production, selected from a malt extract, a flavonoid compound,

a

protein-bound polysaccharide from *Coriolus versicolor*, a paeoniflorin  
 derivative, a tocopherol derivative, and a ferulic acid derivative HSP47 is  
 apparently involved in processing of procollagen to collagen. The composition  
 can efficiently improve the physiol. condition of a patient exhibiting  
 overprodn. of the extracellular matrix, and is useful for preventing or  
 treating various diseases accompanied with abnormal growth of the  
 vascularization. Thus, HSP47 production by human uterus cancer cell line HeLa  
 S3 was inhibited in vitro by paeoniflorin (100 mM),  $\alpha$ -tocopherol (20  
 $\mu$ M), and ferulic acid (100  $\mu$ M).

ST collagen overprodn HSP47 protein inhibitor; extracellular matrix prodn  
 HSP47 protein

IT Neoplasm

(HSP47 formation by cells of; substances inhibiting HSP47 production for  
 treatment of extracellular matrix overprodn.)

IT Glycoproteins, specific or class

RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
 study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES  
 (Uses)

(PS-K; substances inhibiting HSP47 production for treatment of

extracellular matrix overprodn.)

IT Glycoproteins, specific or class  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (collagen-binding, hsp 47; substances inhibiting HSP47 production for treatment of extracellular matrix overprodn.)

IT Rice (*Oryza sativa*)  
 (extract; substances inhibiting HSP47 production for treatment of extracellular matrix overprodn.)

IT Tea products  
 (exts.; substances inhibiting HSP47 production for treatment of extracellular matrix overprodn.)

IT Proteoglycans, biological studies  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (of *Coriolus versicolor*; substances inhibiting HSP47 production for treatment of extracellular matrix overprodn.)

IT Peony (*Paeonia*)  
 (root extract; substances inhibiting HSP47 production for treatment of extracellular matrix overprodn.)

IT Malt  
*Trametes versicolor*  
 (substances inhibiting HSP47 production for treatment of extracellular matrix overprodn.)

IT Flavanols  
 Flavonoids  
 Tocopherols  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (substances inhibiting HSP47 production for treatment of extracellular matrix overprodn.)

IT Antibodies  
 RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)  
 (to heat shock protein HSP47; substances inhibiting HSP47 production for treatment of extracellular matrix overprodn.)

IT 59-02-9,  $\alpha$ -Tocopherol 117-39-5, Quercetin 153-18-4,  
 Rutin 490-46-0, Epicatechin 491-67-8, Baicalein 863-03-6,  
 Epicatechin gallate 970-74-1, Epigallocatechin 989-51-5,  
 Epigallocatechin gallate 1135-24-6, Ferulic acid 1135-24-6D, Ferulic acid, derivs. 23180-57-6, Paeoniflorin 23180-57-6D, Paeoniflorin, derivs.  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); **BIOL (Biological study); USES (Uses)**  
 (substances inhibiting HSP47 production for treatment of extracellular matrix overprodn.)